ARTICLES

Eccentric Exercise in Patients with Chronic Health Conditions: A Systematic Review

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ABSTRACT

Purpose: The capacity of eccentric actions to produce muscle hypertrophy, strength gains, and neural adaptations without stressing the cardiopulmonary system has led to the prescription of eccentric training programmes in patients with low tolerance to exercise, such as elders or those with chronic health conditions. The purpose of this systematic review was to analyze the evidence regarding the effectiveness and suitability of eccentric training to restore musculoskeletal function in patients with chronic diseases.

Summary of Key Points: Relevant articles were identified from nine databases and from the reference lists of key articles. Articles were assessed to determine level of evidence and scientific rigour.

Nine studies met the inclusion criteria. According to Sackett's levels of evidence, 7 studies were graded at level IIb, 1 study at level IV, and the remaining study at level V. Articles were also graded for scientific rigour according to the PEDro scale. One study was rated as high quality, 4 studies were rated as moderate, and 2 studies were graded as poor quality.

Conclusions: Eccentric training may be safely used to restore musculoskeletal function in patients with some specific chronic conditions. However, the heterogeneity of diseases makes it very difficult to extrapolate results and to standardize clinical recommendations for adequate implementation of this type of exercise. More studies are needed to establish the potential advantages of eccentric training in chronic conditions.

Key Words: atrophy, chronic disease, eccentric training, muscle dysfunction

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RÉSUMÉ

Objectif: La capacité des actions excentriques de produire l'hypertrophie musculaire, une masse osseuse accrue et des adaptations neurales sans exercer de fatigue sur le système cardiopulmonaire a mené à la prescription de programmes d'entraînement excentrique chez les patients ayant une tolérance faible à l'exercice, comme les aînés ou ceux qui sont atteints d'états de santé chroniques. Cette étude méthodique a pour but d'analyser les preuves scientifiques concernant l'efficacité et la pertinence de l'entraînement excentrique dans le rétablissement de la fonction musculosquelettique chez les patients atteints de maladies chroniques.

Résumé des points clés: Des articles pertinents ont été identifiés à partir de 11 bases de données et listes de référence d'articles clés. Les articles ont été évalués afin de déterminer le niveau de preuves scientifiques et la rigueur scientifique. Neuf études ont satisfait aux critères d'inclusion. Selon les niveaux de preuve de Sackett, sept études ont été classées au niveau IIb, une étude au niveau IV et la dernière étude au niveau V. Des articles ont aussi été classés pour leur rigueur scientifique selon l'échelle PEDro. Une étude a été classée comme étant de haute qualité, quatre études comme étant de qualité moyenne et deux études ont été classées comme étant de qualité médiocre.

Conclusions: L'entraînement excentrique peut être utilisé en toute sécurité pour rétablir la fonction musculosquelettique chez les patients atteints d'états chroniques spécifiques. Cependant, l'hétérogénéité des maladies rend très difficiles l'extrapolation des résultats et la standardisation des recommandations cliniques pour l'application adéquate de ce type d'exercice. Plus d'études sont requises pour établir les avantages potentiels de l'entraînement dans le cadre des états chroniques.

Mots clés: atrophie, maladie chronique, entraînement excentrique, dysfonction musculaire

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BACKGROUND

Eccentric (lengthening) actions are characterized by elongation of the muscle during active contraction. Greater forces can be produced during eccentric contractions than during concentric (shortening) actions.[1–5] However, the metabolic cost of negative work (e.g., downhill walking) is much less than that of positive work (e.g., uphill walking).[6] For instance, several studies have reported reduced cardiorespiratory and haemodynamic responses when eccentric exercise is compared to concentric exercise at the same absolute workload.[7–12] These results are consistent with investigations illustrating a relatively low ATP turnover and a reduced concentration of metabolites, such as ammonia and lactate, during negative work.[13]

Different theories have attempted to explain this lower metabolic cost. The current view is that there is a greater contribution of elastic components in the muscle-tendon complex during eccentric actions, thus increasing the potential of force production at reduced energy expenditure.[14–16] Skeletal muscle has a great capacity to absorb mechanical energy during eccentric actions, and a large proportion of this stored energy is reused to reduce the active force requirements in the subsequent concentric muscle contraction.[17] The reduced surface electromyographic (EMG) activity of muscles performing eccentric actions is consistent with the postulated superiority of the mechanical efficiency of these muscle contractions.[18]

The intensity of the muscle contraction seems to be an important stimulus for muscle growth and strength development,[19] and, therefore, the greater capacity of eccentric actions to produce force has received the attention of many investigators, who have explored the effectiveness of eccentric exercise regimens in enhancing skeletal muscle performance.[20] Although muscle adaptations observed after training tend to be contraction-specific,[21,22] it is generally accepted that exercise protocols in which eccentric actions are emphasized produce more important gains in strength,[23,24] muscle mass[25,26] and neural adaptations[27,28] than regimens consisting of concentric actions only. Moreover, when eccentric and concentric contractions are performed at the same metabolic level (i.e., oxygen consumption), eccentric-biased interventions result in greater strength gains and muscle fibre hypertrophy.[29] The lower metabolic, neural, and cardiorespiratory cost of eccentric actions,[30] combined with the relative preservation of eccentric force expression during ageing,[31] has led to the prescription of this type of training programme for individuals with reduced tolerance for physical activity.[32] For example, eccentric training has been demonstrated to be effective in increasing muscle mass and strength and reducing fall risk in the elderly.[33] Similarly, others have reported increased strength gains and neuromuscular adaptations after eccentric training compared to a conventional protocol consisting primarily of concentric actions.[30] It is noteworthy that recent studies have used elevated training intensities with eccentric contractions to restore musculoskeletal function in patients with different chronic diseases.[34–36]

Musculoskeletal dysfunction is relatively common in patients with chronic conditions such as chronic obstructive pulmonary disease,[37,38] chronic heart failure,[39,40] and stroke.[41,42] This decline in muscle function reduces functional mobility and physical capacity, which, in turn, can result in a limited ability to maintain muscle activity and decreased levels of protein synthesis.[43–46] However, the exact aetiology of this deterioration is not yet clear. Disease-specific factors that cause muscle impairment (e.g., oxidative stress) may be related to the nature of the pathophysiologic changes that affect the target organ. However, given that most of these patients have multiple chronic conditions, the specific factors initiating muscle deterioration and atrophy are difficult to determine. The aetiology of the dysfunction (i.e., neural, metabolic, mechanical), the patient's characteristics (age, gender), the disease severity, and even the type of treatment received (e.g., exercise, drugs) may interact synergistically to induce muscle pathology and atrophy. The extent to which each of these factors affects muscle activity is uncertain. However, it is believed that some of the deleterious changes observed in the muscles of these patients are not only produced by the disease per se but are also due to the lack of physical activity commonly observed with ageing. The improvements in muscle function observed in older adults enrolled in resistance training programmes partially support this view.[47,48] Trials comparing muscle characteristics of highly trained young and senior athletes have shown that trained subjects can indeed maintain and improve muscle function regardless of their age.[49] Therefore, it is likely that physical inactivity plays an important role in reducing overall muscle function in some patients with chronic diseases as well. Moreover, the effectiveness of exercise in maintaining mobility and minimizing muscle wasting in most people with chronic conditions is, at this point, indisputable.[50,51] Likewise, the design of new strategies to prevent muscle atrophy and declines in strength, endurance, and coordination in these diseases requires further exploration.

To our knowledge, a review regarding the application of eccentric exercise to restore musculoskeletal function in persons with chronic conditions has not yet been conducted. Given the potential application of this type of exercise in patients with low exercise tolerance, we decided to perform a systematic review that included populations with different chronic health conditions to determine whether there were commonalities and disease-specific issues related to eccentric exercise prescription. Therefore, the main aim of the present systematic review was to explore the current evidence regarding the effectiveness and suitability of eccentric exercise in restoring musculoskeletal function in patients with different chronic conditions.

METHODS

Search Strategy

The literature search included articles from the following databases: Cochrane Controlled Trials Register, MEDLINE, CINAHL (Cumulative Index to Nursing and Allied Health Literature), EMBASE, SPORTDiscus, Web of Science, PEDro (Physiotherapy Evidence Database), Proquest theses, and PapersFirst. Reference lists from key articles related to the topic were also reviewed. Only studies written in English were included, and the literature search was restricted to the years between 1966 and 2006. The search was initially supervised by a health sciences reference librarian, who helped to define the criteria in order to find as many sources of information as possible. The key words used to perform the search were "eccentric training," "eccentric contraction," "eccentric exercise," "excentric contraction," "lengthening contraction," "pliometric contraction," "pliometric action," and "negative work." These search terms were chosen because they have traditionally been used to describe eccentric training or eccentric contraction. The results of this primary search were then combined with the following chronic clinical conditions: "respiratory disease" ("chronic obstructive pulmonary disease," "emphysema," "chronic bronchitis," "cystic fibrosis," "bronchiectasis," "asthma"), "neurological disease" ("stroke," "Parkinson's disease," "multiple sclerosis," "poliomyelitis") "cardiovascular disease" ("chronic heart failure," "coronary artery disease," "cardiomyopathy"), "muscle dystrophy," "osteoarthritis," "rheumatoid arthritis," "osteoporosis," "diabetes," "renal disease," "cancer," "obesity." These conditions were selected based on the following definition: "Chronic diseases are those which are permanent, leave residual disability, are caused by non-reversible pathological alteration, require special training of the patient for rehabilitation, or may be expected to require a long period of supervision, observation, or care."[52] Two reviewers performed the data search independently, using the same procedures. The two reviewers compared their search results, and studies were included for review according to the study-selection criteria.

Study Selection

Studies selected for inclusion were those in which (1) patients were affected by some of the chronic diseases previously defined;[52] (2) a specific and well-defined component of eccentric exercise was included; (3) eccentric training was performed at least twice a week, for a minimum of 4 weeks—training was considered only when it involved at least 2 sets of 10 repetitions per targeted muscle and per session (resistance training) or lasted a minimum of 20 minutes (endurance training); and (4) the minimum age of the patients was set at 18 years. No limitations regarding the type of study design were applied. Studies excluded from the review were those in which (1) subjects were affected by other potential co-morbidities not included in the definition of chronic disease,[52] or had acute conditions (e.g., muscle strains) or overuse injuries (e.g., chronic Achilles tendinosis); (2) eccentric exercise was not clearly defined as the primary component of the intervention for at least 1 study group (e.g., studies in which concentric and eccentric protocols were not provided separately or in which the eccentric phase of the movement was not sufficiently emphasized); or (3) interventions did not meet the minimum inclusion criteria in terms of training design (volume, frequency, length).

Data Extraction

Two independent reviewers performed the data extraction, analyzing the characteristics of each study that met the inclusion criteria. Standardized forms specifically created for the purposes of the review were used. After the data were extracted, the two reviewers compared their results. In cases of disagreement, a third reviewer was included in the discussion until consensus was obtained.

Review Criteria

In the present review, Sackett's initial rules of evidence,[53] as described by the Oxford Centre for Evidence-Based Medicine, were used to evaluate the level of confidence provided by the results of the selected studies.[54,55] This adaptation of Sackett's initial rules of evidence allows a more detailed categorization of the different levels of evidence according to the characteristics of the study design and the control of potential threats to internal validity.[56] To assess interrater reliability, all

Table 1 Sackett's Initial Rules of Evidence, as Described by the Oxford Centre for Evidence-Based Medicine[54]

Level of Evidence	*Type of Study*
I	(a) systematic review (homogeneous) of high quality RCTs (b) individual high-quality RCTs (c) all or none
II	(a) systematic review (homogeneous) of cohort studies (b) individual cohort study, including low-quality RCTs (c) "outcomes" research
III	(a) systematic review of case-control studies (b) individual case-control studies
IV	case series (no control group) and low-quality cohort and case-control studies.
V	expert opinion and single-subject design studies

selected studies were scored by two independent raters.[57] Any disagreements were discussed until consensus was achieved, and in the event that differences could not be resolved, a third reviewer scored the study. Sackett's initial rules of evidence, as used in this review, are shown in Table 1.

Methodological Quality of Reviewed Studies

There are many examples of different quality-assessment tools in the literature, but we decided to use the PEDro scale,[58] because the scoring items appeared well suited to evaluate studies within the realm of rehabilitation and also because it has previously shown good reliability.[59,60] This scale was originally adapted from the Delphi list for quality assessment of randomized controlled trials (RCTs) for conducting systematic reviews[61] and is based on the following 11 items relating to scientific rigour: eligibility criteria, random allocation, concealed allocation, follow-up, baseline comparability, blinded subjects, blinded therapists, blinded assessors, intention to treat, between-groups analysis, and both point and variability measures. All items except 1 (eligibility criteria) were used to calculate the final score (maximum 10 points). This item was excluded because it affects external but not internal or statistical validity.[58] A study was considered to be of high quality if its PEDro score was greater than 5, of moderate quality if the score was 5 or 4, and of low quality if it scored 3 or lower. The scientific rigour of the selected articles was independently assessed by two reviewers, and the interrater reliability of the PEDro scale was evaluated using the intraclass correlation coefficient (ICC Type 2,1),[57] calculated on the total scores. In cases of disagreement, as in the process of determining the different levels of evidence, a third reviewer was included in the scoring process to reach a final consensus.

Effect Size

To determine the effectiveness and suitability of eccentric training in improving some relevant musculoskeletal aspects affecting patients with chronic diseases, the effect size for comparable outcome measures was calculated. The effect size index (d) is defined as the degree of differences between groups and was calculated by dividing the difference between group means by the average standard deviation of the groups.[57] The different levels of interpretation of this index were categorized according to the criteria established by Cohen: large effect ($d > 0.8$), moderate effect ($0.2 < d < 0.8$), and small effect ($d < 0.2$).[62] When numerical comparisons were not possible, differences between trials were evaluated descriptively by exploring study population, types of interventions, and outcomes.

RESULTS

The primary search strategy led to a large number of studies ($N = 69$). Nevertheless, many of the articles initially found were subsequently excluded because neither the title nor the abstract contained relevant information on the topic of this review. In the end, only nine studies met the inclusion criteria.[34–36,63–68] The main reasons for exclusion were (1) that eccentric interventions were not provided separately or were not sufficiently emphasized and (2) that the targeted population was not affected by any specific chronic condition. For instance, some studies exploring the potential use of eccentric protocols in elderly individuals were not included in the data analysis because the specific diseases of the patients were not reported[69] or because aspects such as sarcopenia,[70] fall risk, and frailty[33] were associated with the ageing process rather than with chronic disease. Seven articles used an experimental design that compared eccentric and concentric interventions.[35,36,63–65,67,68] The outcomes, however, varied substantially depending on the clinical conditions studied. In addition, a case report[66] and a one-group quasi-experimental design study[34] were also included. Three studies were related to coronary artery disease,[36,64,67] two to Parkinson disease,[34,65] and one each to chronic obstructive pulmonary disease,[65] osteoarthritis,[35] and stroke.[68] It should be noted, however, that two of the studies involving persons with coronary artery disease,[36,64] and both studies of persons with Parkinson disease,[34,65] used the same group of subjects in each of the two sets of studies (personal communication with study authors). Because it met all the inclusion criteria, one article in which eccentric training was used in patients with polymyositis was also included.[66] In six of these articles,[34,36,63–65,67] eccentric training was provided through a custom-built, specially designed, motor-driven ergometer, whereas isokinetic ergometers were used in the three remaining studies.[35,66,68] A more detailed description of the studies is presented in Table 2.

Levels of Evidence

Interrater agreement on the levels of evidence for the articles chosen was 100%. Likewise, both independent reviewers categorized the selected articles following the same criteria. Seven articles were rated at level IIb (low-quality RCTs) because of their small sample sizes and the weakness of their results. [35,36,63–65,67,68] One of the two remaining articles was allocated to level IV, since no control group (i.e., concentric group) was included (one-group, pretest–posttest design),[34] and the last article was rated at level V, as it was a case report.[66] Levels of evidence for each study are reported in Table 2.

Table 2 Main Characteristics of the Studies Included in the Systematic Review, Including Levels of Evidence

Study	*Design*	*Sackett's Level of Evidence*	*Disease*	*Sample Size and Gender*	*Age*	*Intervention Groups (n patients)*	*Duration*	*Frequency*	*Outcome Measures*	*Effect Size*	*Results*
Rooyackers et al. (2003)[63]	RCT	IIb	COPD	20 m, 4 w	36–72	GT ($n = 12$): dynamic and isometric exercises, 20 min interval cycling (2 min rest + 2 min exercise) GT+ Ecc ($n = 12$): dynamic and isometric exercises, 20 min interval cycling (2 min rest + 2 min exercise) + progressive eccentric cycling up to 15 min	10 weeks	5 days/ week	Work output, cardiorespiratory responses, 6MWD, CRDQ	*Work*: GT = 0.31; GT + Ecc = 0.23 *6MWD*: GT = 0.69; GT + Ecc = 0.87 *CRDQ*: GT = 0.90; GT + Ecc = 0.78	Some cardiopulmonary parameters (HR and gas exchange) improved only slightly in Ecc protocol. Patients in Ecc group were able to maintain higher work loads at reduced RPE. Work output was not significantly different between groups. GT + Ecc group slightly improved 6MWD, but GT was slightly better in the CRDQ.
Meyer et al. (2003)[64]	RCT	IIb	CAD	13 m	40–66	Ecc ($n = 7$): eccentric cycling (30 min at 65% VO_2peak) Con ($n = 6$): concentric cycling (30 min at 65% VO_2peak)	8 weeks	3 days/ week	Work output, cardiorespiratory responses	*Work output*: Ecc vs. Con = 4.45	Similar haemodynamic responses (except for the first 5′ of exercise, when Con protocol elicited lower responses in some haemodynamic parameters using four-fold power output in the Ecc group). Blood lactate accumulation was much lower in the Ecc group during exercise.
Steiner et al. (2004)[36]	RCT	IIb	CAD	12 m	44–60	Con ($n = 6$): concentric cycling (30 min at 60% VO_2peak from week 5) plus comprehensive rehabilitation program (calisthenics, stretching, relaxation) Ecc ($n = 6$): eccentric cycling (30 min at 60% VO_2peak from week 5) plus comprehensive rehabilitation program (calisthenics, stretching, relaxation)	8 weeks	3 days/ week	Muscle mass, strength, fibre size, RPE, work output	*Work output*: Ecc vs. Con = 5.74 *Strength*: Ecc = 4.9% (Isom), 3.2% (Con 60), 2.5% (Con 120); Con = n.s. Muscle mass = n.s. *Fibre size*: Ecc vs. Con = 0.56	Ecc group achieved a three-fold total workout compared to Con group. Strength gains were observed only in the Ecc group (isometric and concentric isokinetic at either faster or slower velocity). Fibre CSA increased only in the Ecc group. RPE related to the LEs was higher in the Ecc group, whereas the Con group showed a higher RPE related to cardiorespiratory effort.
Zoll et al. (2006)[67]	RCT	IIb	CAD	12 m	Not reported	Con ($n = 6$): 30 min concentric cycling at 60% VO_2peak from week 5 Ecc ($n = 6$): 30 min eccentric cycling at 60% VO_2peak from week 5	8 weeks	3 days/ week	Mitochondrial biogenesis and function, contractile phenotype, mechanical stress markers	n.p.	COX-4 mRNA was significantly reduced and Tfam transcript concentration showed a modest drop in the Ecc group. These decreases corresponded to a reduction in total mitochondrial volume density. MyHC IIa transcript was significantly reduced and MyHC I showed a trend toward a reduction in the Ecc group. No differences were found in IGF-I mRNA levels between groups.

Dibble et al. (2006)[65]	RCT	IIb	PD	19	40–85	Ecc ($n=10$): calisthenics, stretching, walking, cycling, lifting weights upper extremities plus high-intensity eccentric cycling (45–60 min) Standard care treatment ($n=9$): calisthenics, stretching, walking, cycling, lifting weights upper extremities (45–60 min)	12 weeks	3 days/ week	Muscle volume, torque, mobility measures, LE pain (VAS), RPE	*Muscle volume*: (Ecc): MALE = 0.27, LALE = 0.26; (Standard): MALE = 0.04, LALE = 0.14 *Torque*: (Ecc): MALE = 0.77, LALE = 0.73; (Standard): MALE = 0.25, LALE = 0.06 *Mobility performance*: (Ecc): 6MW = 0.68, SD = 0.53, SA = 0.41; (Standard): 6MW = 0.20, SD = 0.01, SA = 0.03	Greater increases in muscle volume, muscle force, and functional status in the Ecc group. Minimal LE pain in the Ecc group during the first two weeks; the rate of perceived exertion (RPE) of the LEs increased only from week 1 to week 4 in the Ecc group.
Engardt et al. (1994)[68]	PP	IV	PD	10	40–85	Ecc ($n=10$): eccentric cycling with progressively increased intensity (RPE)	10 weeks	2 days/ week	Torque, muscle activity (EMG), gait, body weight distribution	*Torque*: (Ecc): Ecc(60) = 0.70, Ecc(120) = 0.66, Ecc(180) = 0.63; Con(60) = 0.69, Con(120) = 0.64, Con(180) = 0.60; (Con): Ecc(60) = 0.56, Ecc(120) = 0.64, Ecc(180) = 0.65; Con(60) = 0.62, Con(120) = 0.74, Con(180) = 0.84	Ecc group increased more Ecc and Con strength in the paretic LE compared to the Con group. Antagonistic activity increased after Con training only. Symmetrical body weight distribution in rising from a sitting position only after Ecc training. No differences in gait speed and duration of swing phase.
Dibble et al. (2006)[34]	RCT	IIb	ST	15m, 5w	54–71	Ecc ($n=10$): eccentric isokinetics: repeated sets at different velocities (60–180 deg.s^{-1}) Con ($n=10$): concentric isokinetics: repeated sets at different velocities (60–180 deg.s^{-})	12 weeks	3 days/ week	CK, LE pain, (VAS), isometric force, work output	n.p.	No significant CK concentrations and low pain scores (VAS). Significant increases in isometric force and total power output.

(Continued)

Table 2 Contd.

Study	*Design*	*Sackett's Level of Evidence*	*Disease*	*Sample Size and Gender*	*Age*	*Intervention Groups (n patients)*	*Duration*	*Frequency*	*Outcome Measures*	*Effect Size*	*Results*
Gür et al. (2002)[35]	RCT	IIb	OA	23	41–75	Con ($n=9$): 12 reps knee extensors-flexors Con/Ecc ($n=8$): 6 + 6 reps knee extensors-flexors Non-treatment ($n=6$)	8 weeks	3 days/ week	Functional capacity, pain at rest and during activities (VAS), peak torque, CSA of knee muscle groups	*Total functional capacity*: (Ecc/Con) = 1, (Con) = 0.88 *Pain*: greater in Ecc group *CSA*: n.s. Con vs. Ecc/Con *Strength*: n.s. Con. vs Ecc/Con	Both training groups increased CSA and torque of knee muscles, increased functional capacity, and reduced pain scores. The Ecc/Con group showed more improvements in functional capacity, whereas the Con group showed more reduced pain scores. Non-treatment group did not show significant differences between pre- and post-tests.
Harris-Love (2005)[66]	ICR	V	PM	1m	64	Ecc ($n=1$): eccentric isokinetics: 1 week familiarization (2 sets at 80–90% RM); 2–3 weeks acclimatization (2–3 sets at 110–120% RM); 4–12 weeks progression (130–140% RM)	12 weeks	2 days/ week	Peak torque knee extensors, DOMS (VAS), passive ROM, serum enzyme levels	n.p.	No exacerbation of serum enzyme levels; DOMS evaluated using VAS was non-significant. The post-training isometric and isokinetic measurements increased 48.8% and 52.6% respectively. Ability to rise from a low surface improved slightly, but the rate of fall remained unchanged.

Design: ICR = individual case report; PP = non-controlled pretest–posttest design; RCT = randomized controlled trial

Disease: CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; OA = osteoarthritis; PD = Parkinson disease; PM = polymyositis; ST = stroke

Intervention: Con = concentric exercise; Ecc = eccentric exercise; GT = general training; RM = repetition maximum

Effect Size: Con(60) = Concentric isokinetic torque at 60°/second; Con(120) = Concentric isokinetic torque at 120°/second; Isom = isometric peak; LALE = less affected lower extremity; MALE = most affected lower extremity; SD = stair descent; 6MW = 6-minutes walk test; n.p. = not provided; n.s. = non-significant

Outcome Measures and Results: CK = serum creatine kinase; CRDQ = chronic respiratory disease questionnaire; CSA = cross-sectional area; DOMS = delayed-onset muscle soreness; EMG = electromyography; IGF-1 = insulin-like growth factor 1; LE = lower extremity; MyHC = myosin heavy chain; ROM = range of motion; RPE = rating of perceived exertion; VAS = visual analogue scale; VO_2 = oxygen consumption; 6MWD = 6 minutes walking distance test

Methodological Quality

The PEDro scoring system was used only for those 7 studies in which at least two groups were compared.[35,36,63–65,67,68] The ICC (type 2,1) to measure inter-rater reliability of the PEDro scale in these studies was poor to moderate (0.68).[57] According to the PEDro rating system, the scientific quality of the studies was categorized as low for 1 study,[64] moderate for 5 studies,[35,36,63,67,68] and high in only 1 study.[65] The final scores ranged from 3 to 6 points; 5 was the most frequent score (occurring 3 times). The most common flaw was a lack of blinding of subjects, therapists, or assessors. In addition, those items related to the subjects' allocation into groups were usually scored poorly because the allocation method was not concealed. A detailed description of the PEDro scores for the studies evaluated can be seen in Table 3.

Effect Size

The effect size of the main outcomes was calculated only for studies that provided raw data. The effect size was not calculated for two trials[34,66] in which, because of their design, there was no comparison between groups. Since one study reported exclusively cellular adaptations after eccentric and concentric training,[67] the effect size for the outcomes of this study was not calculated. In addition, authors of two studies had already reported effect-size calculations for their main outcomes.[35,65] In general, eccentric training showed larger effect sizes in terms of work production during exercise[64,36] and slightly better outcomes in functional measurements.[63,65,35] The effect sizes for the most relevant outcomes of each study are shown in Table 2.

DISCUSSION

The main finding of this systematic review is that very few studies exploring the use of eccentric-biased programmes in persons with chronic health conditions have been conducted. Furthermore, using the PEDro scale, the scientific rigour of the majority of these studies was rated as "moderate" (71.5%) or "low" (12.9%). In particular, failure to blind subjects, assessors, and therapists, as well as a lack of intention-to-treat analysis, reduced the quality of all the studies. However, it is important to take into account that, in these types of studies, blinding of subjects and even of therapists is very difficult. Because so few available studies met our inclusion criteria, we included the two low-quality studies that explored the use of eccentric exercise in two neurological conditions.[34,66] Given the small number of studies, it was impossible to determine whether there were commonalities and disease-specific issues related to eccentric exercise prescription. Furthermore, the use of different

Table 3 Detailed PEDro Scores of the Group Studies Included in the Systematic Review

Study	*Random Allocation*	*Concealed Allocation*	*Baseline Comparability*	*Assessors Blinded*	*Subjects Blinded*	*Therapists Blinded*	*Follow-Up*	*Intention to Treat*	*Between-Groups Analysis*	*Point Estimates and Variability*	*Total Score*
Rooyackers et al. 2003[63]	Y	N	Y	N	N	N	N	N	Y	Y	4
Meyer et al. 2003[64]	Y	N	N	N	N	N	N	N	Y	Y	3
Steiner et al. 2004[36]	Y	N	Y	N	N	N	Y	N	Y	Y	5
Zoll et al. 2006[67]	Y	N	Y	N	N	N	Y	N	Y	Y	5
Dibble et al. 2006[65]	Y	Y	Y	N	N	N	Y	N	Y	Y	6
Gür et al. 2002[35]	Y	N	Y	N	N	N	Y	N	Y	Y	5
Engardt et al. 1994[68]	N	N	Y	N	N	N	Y	N	Y	Y	4

Y = Yes; N = No

Random allocation: The allocation method must be clearly stated.

Concealed allocation: Refers to whether the person who determined subjects' eligibility for inclusion in the trial was aware, at the time he or she made her decision, which group the next subject would be allocated to.

Subjects blinded: Blinding was considered to have occurred when it was specifically described or when a sham intervention (placebo) for the control group was specifically used.

Follow-up: A "Yes" indicates that measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups.

Intention to treat: Defined as the principle whereby data are analyzed according to group assignments, regardless of how subjects actually received treatment. In other words, the data have been analyzed assuming that each patient received the treatment to which he was assigned.

training modalities, such as resistance (i.e., eccentric isokinetic)[35,66,68] training and endurance training (i.e., eccentric cycling),[34,36,63–65,67] reduced comparability among studies in terms of exercise prescription.

Some of the studies provided modest levels of evidence,[35,36,63–65,67,68] and therefore, according to these results, the clinical application of eccentric training in persons with chronic health conditions must be considered very cautiously. However, eccentric protocols showed an overall increased capacity to produce work output at relatively lower metabolic intensities;[36,63,64] that is, much more work was produced by patients performing eccentric training, even though physiologic intensity (i.e., oxygen consumption) was the same in both groups. Furthermore, eccentric training was performed without some of the adverse responses commonly attributed to this type of muscle action (e.g., muscle soreness). Studies in which muscle soreness and rate of perceived exertion were examined demonstrated that when eccentric training is implemented progressively, it does not increase muscle discomfort or subjective fatigue.[34,65] In addition, in two of the studies that evaluated functional performance, eccentric protocols showed a slightly greater capacity to improve tasks involving coordination and movement control.[35,65] In spite of these functional improvements, one should be cautious not to extrapolate these gains to persons with other clinical conditions.

Cardiorespiratory Diseases

Despite the limited number of studies exploring the use of eccentric training in persons with respiratory[63] or cardiovascular[36,64,67] chronic conditions, the physiologic characteristics of this type of muscle contraction seem to be well suited for incorporation into the training of these patients. For instance, a recent study has shown that resistance training may lead to increases in arterial stiffness and pulse pressure.[71] On the other hand, eccentric training seems to mitigate reductions in arterial compliance,[72] thus potentially reducing the risks commonly associated with resistance training in patients with coronary disease. In addition, cardiopulmonary stress is attenuated during eccentric exercise, and the lower metabolic cost as well as the potential stimulus for muscle growth from eccentric actions have been documented[29] even in older adults.[30,70] However, the adequate prescription of eccentric training for these patients requires more investigation. Some studies not included in this review have revealed disproportionate increases in breathing frequency during the initial stages of the negative exercise in healthy individuals.[12] Obviously, this might have deleterious consequences for patients with cardiorespiratory conditions such as coronary artery disease and chronic obstructive pulmonary disease.

In addition, other studies have shown that there are important differences in some acute haemodynamic responses (initial 5 minutes) when eccentric and concentric exercise are compared.[10] Since peripheral muscle activation plays an important role in regulating sympathetic nerve activity, it is likely that the neurological patterns regulating these responses are different depending on the characteristics of the muscle contraction performed.[73] Furthermore, although classical studies did not show differential effects on muscle capillarity and enzyme concentration between eccentric and concentric training,[74] some recent findings have reported contraction-specific molecular responses[75] and cellular signalling pathways[67] regulating the oxidative properties of skeletal muscle. Combined, these findings suggest important differences in terms of training adaptations, depending on the type of muscle contraction emphasized during exercise.

Given the mechanical characteristics of lengthening actions (i.e., mechanical energy is stored as heat in the working muscles), some studies have reported increases in core temperature during eccentric training (0.7°C) as compared to concentric training.[76] Although other studies did not find such physiologic responses,[77] the potential adverse effects of increased temperature on the thermoregulatory system during eccentric work should be considered in patients with altered cardiorespiratory function.[78] Given the importance of maintaining muscle oxidative potential while reducing cardiopulmonary stress in such patients, these aspects should be addressed in future studies.

Neurological Diseases

The role of eccentric training in neurological conditions is controversial. Only three articles involving persons with chronic neurological diseases met inclusion criteria for the present review.[34,65,68] Moreover, in the two studies related to patients with Parkinson disease,[34,65] the training groups involved the same subjects. However, in spite of traditional theories of neurorehabilitation in which strength training was completely avoided, the current view is that judicious resistance-training programmes may improve muscle function[79] and even functional task performance[80] in patients with some neurological disorders. In a recent review on the use of resistance training in persons with stroke, the authors reported that protocols including a specific component of eccentric exercise yielded greater strength gains than conventional training routines.[81] The study of survivors of stroke included in the present review partially supports this view.[68] In that study, Engardt et al. showed that eccentric contractions induced more significant gains in strength after the paretic leg of these patients was trained. According to these authors, the potential advantage of eccentric exercise in persons with stroke may be explained by the capacity of eccentric contractions to circumvent the limitation of force production via inhibition of antagonist co-contraction and activation of stretch reflexes.[68] That is, while concentric training increases antagonist activity, antagonist co-contraction is lower and the stretch reflex is increased during eccentric movements.[82] Both phenomena might theoretically enhance the capacity to produce force while the muscle is being lengthened.

Although the different biophysical muscle adaptations from long-term eccentric exercise have been well documented,[83] the effects of this type of training in several other aspects related to muscle function, such as movement control, have not been sufficiently studied. For instance, the impact that the potential increase in passive muscle stiffness observed after some weeks of eccentric cycling[15] may have on the functional performance of patients with reduced functional mobility is uncertain. Even though eccentric contractions seem to follow a very specialized neural pattern, possibly aimed at protecting muscle from being disrupted,[1] the long-term implications of this type of training on the control and execution of functional movements remain to be elucidated. For instance, Barry et al. have suggested that the neural specificity of eccentric contractions would limit the transferability of strength gains from eccentric training to functional tasks performed concentrically or isometrically.[84] In addition, the deleterious influence that the increased core temperature observed during negative work[76] might have in patients with some neurological conditions, such as multiple sclerosis, should be taken into account.[50]

Musculoskeletal Diseases

No studies using eccentric protocols in patients with osteoporosis were found. However, other studies not included in the data analysis provide relevant information about the potential application of eccentric training in patients with osteoporosis. For instance, it has been observed that there is a moderate correlation between muscle strength and bone-mass density after one year of resistance training.[85] Given the greater muscle tension and strength gains observed after eccentric training,[23–28] it has been hypothesized that eccentric actions might be effectively used in patients with reduced bone mass. Exploring this hypothesis, Hawkins et al. reported increased site-specific bone density using eccentric contractions after 18 weeks of resistive training in young women. [86] Interestingly, in this study the concentrically trained lower extremity did not show the same osteogenic response, indicating that the greater force production (load magnitude) using lengthening muscle actions is a determinant in increasing bone density from muscle activity. Other studies using animal models support this view[87] and warrant further investigations analyzing the optimal intensity of this type of training to increase bone mass, not only in healthy individuals[88] but also in patients with osteoporosis.

In contrast, the additional benefits that eccentric-biased exercise might bring to the management of osteoarthritis are equivocal. In one study included in this review, Gür et al. showed that, using the same repetitions, eccentric/concentric training was superior to concentric training alone in terms of functional improvement in patients with knee osteoarthritis.[35] Nevertheless, the concentric protocol was more effective in terms of pain management. Therefore, the advantage of including eccentric muscle actions in the rehabilitation of these patients is still unclear.

Myopathic Diseases

Only one study that used eccentric training in muscle diseases was included in the present review.[66] However, this study is an individual case report, representing the lowest level of evidence, and the results should therefore be regarded with caution. In spite of new findings suggesting that one bout of eccentric contractions does not exacerbate markers of muscle damage in patients with slowly progressive muscular dystrophies, such as myotonic muscular dystrophy,[89] the use of intensive eccentric contractions in patients with increased susceptibility to muscle injury, such as those with Duchenne muscular dystrophy, should be avoided.[90,91] Studies using animal models of muscular dystrophy have shown that high-intensity eccentric contractions may indeed have deleterious effects on muscle integrity, especially in older muscles with limited capacity for regeneration.[92] Whereas the use of light resistance training consisting primarily of concentric actions may bring about some benefits, eccentric training does not seem to be appropriate to restore muscle function in these patients.

Metabolic Diseases

No studies meeting the inclusion criteria were found regarding the use of eccentric exercise in patients with metabolic disorders such as diabetes. However, one interesting study reported preliminary data suggesting that eccentric training improves glucose tolerance more than concentric training.[93] More investigations are needed to confirm these results.

Study Limitations

This systematic review has several limitations that should be considered. The main limitation is related to the small number of studies that met the inclusion criteria. One potential explanation for this is the novelty of this approach and the limited availability of eccentric ergometers for use in rehabilitation, as illustrated by the fact that the eccentric devices used in most of the trials were very similar (created from an original model)[94] and were specifically designed for these studies. Moreover, since eccentric contractions have traditionally been associated with muscle damage, this may have discouraged the development of these protocols in clinical practice. In addition, the clinical heterogeneity of the studies included in the analysis limited the power of the review. Because of the variety of outcomes, the power of the studies was not increased by pooling the data or through meta-analysis, and, therefore, some observed differences across studies were merely described. However, given that the initial purpose of our study was to determine whether there were commonalities and disease-specific issues related to eccentric exercise prescription, this variability was expected.

Another important limitation is related to the type of exercise performed and how this influenced interpretation of the results. In some studies, participants undertook eccentric resistance protocols (i.e., isokinetic), whereas in others, eccentric endurance training (i.e., cycling) was provided. Although we did not differentiate between these two approaches, it is well known that training adaptations are quite specific depending on the type of exercise performed (i.e., resistance vs. endurance). Unfortunately, the limited number of studies made it impossible to classify them according to the type of training protocol used. In addition, the potential use of high-intensity loads in eccentric cycling makes it very complicated to simply define this exercise as endurance training. Despite the use of some specific training parameters (e.g., weeks of training) to exclude trials studying only acute responses from eccentric exercise (e.g., responses after one or several bouts performed the same day), it is always complicated to establish for how much time an exercise should be performed to be considered "training" and what is the exact point at which training adaptations become chronic. In future investigations, these differences might be avoided by using more accurate descriptors to define each type of training modality.[95]

Despite the efforts made to include only studies in which the eccentric part of the movement was isolated, this was not always possible. Both eccentric and concentric actions are repeated cyclically during normal human locomotion, and, therefore, it is difficult to isolate one phase from the other. For instance, in the studies in which the eccentric ergometer was used,[34,36,63–65,67] subjects performed both muscle actions, although the negative part of the movement was much more emphasized. Therefore, adaptations cannot be attributed exclusively to the eccentric component of the movement. In contrast, the studies that used an isokinetic device[35,66,68] almost completely suppressed the concentric phase of the movement in the eccentric group, and the potential adaptations were produced exclusively by the eccentric stimulus.

CONCLUSIONS AND IMPLICATIONS FOR FUTURE RESEARCH

This systematic review has shown that the evidence for the use of eccentric contractions in persons with chronic health conditions is very limited. Furthermore, whereas eccentric training seems to be well suited for individuals with diseases in which cardiopulmonary stress is a limiting factor for exercise, the role of this muscle contraction in other chronic conditions is unclear. However, this review has shown relevant aspects related to this type of exercise that merit further exploration. For instance, the relative conservation of eccentric force in older individuals[31] and in those with certain chronic conditions, such as chronic obstructive pulmonary disease[96] and stroke,[97] by comparison to either isometric or concentric force makes this contraction a potential tool for restoring muscle function in patients with chronic diseases. The reduced initial levels of force lead these individuals to experience difficulties in taking part in rehabilitation programmes. The use of eccentric training might circumvent this initial limitation. In addition, the great capacity of eccentric contractions to induce muscle gains and neural adaptations at a reduced metabolic level has been demonstrated.[29] Unfortunately, there is no consensus on the ideal prescription of this type of exercise in patients with low tolerance to exercise to avoid the potential adverse effects of unaccustomed eccentric training and to account for differences in response between women and men.[98] Given that eccentric training can produce deleterious effects[99] and that recovery from this type of exercise is impaired with age,[100] efforts should be made to investigate the different factors regulating muscle damage and adaptation after eccentric training in these patients.

In summary, future studies should investigate the use of eccentric muscle actions in persons with different chronic diseases. If eccentric training were shown to be effective, a second step would involve the creation of standardized protocols based on specific conditions and patient characteristics. In addition, the postulated preservation of eccentric force, its exact origin (i.e., neural or mechanical), and whether it is a commonality in all chronic conditions should be explored. The impact of eccentric-biased protocols on functional performance requires further study. The study of the neurological pathways regulating transferability from eccentric versus concentric training to task execution is an exciting area for further research. Finally, efforts should be made to design eccentric devices that can be used routinely in clinical rehabilitation settings.

KEY MESSAGES

What Is Already Known on This Subject

During eccentric muscle actions skeletal muscle generates greater levels of force, with a reduced metabolic, haemodynamic, and cardiorespiratory cost, than concentric contractions. This efficiency of eccentric actions can be used to restore musculoskeletal function without stressing the cardiopulmonary system. From a physiologic perspective, the implementation of eccentric actions in rehabilitation programmes for people with low tolerance to exercise, such as those with chronic health conditions, can have some advantages over conventional training protocols emphasizing concentric actions.

What This Study Adds

Eccentric training can be safely implemented in the training routines of some chronic diseases. The evidence shows that especially some cardiorespiratory and neurological conditions can potentially take advantage of this type of training. However, more studies are needed to establish the potential benefits of eccentric training in chronic health conditions. The specificity of each chronic disease makes it very difficult to establish standardized protocols for this type of training. Despite being attractive as a new therapeutic modality, the adequate prescription of eccentric training in chronic health conditions requires further investigation.

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REFERENCES

1. Enoka R. Eccentric contractions require unique activation strategies by the nervous system. J Biomech. 1996;30:447–55.
2. Jones DA, Rutherford, OM. Human muscle strength training: the effects of three different regimes and the nature of the resultant changes. J Physiol. 1987;391:1–11.
3. Komi PV, Buskirk ER. Effect of eccentric and concentric muscle conditioning on tension and electrical activity of human muscle. Ergonomics. 1972;15:417–34.
4. Seliger V, Dolejs L, Karas V. A dynamometric comparison of maximum eccentric, concentric, and isometric contractions using EMG and energy expenditure measurements. Eur J Appl Physiol. 1980;45:235–44.
5. Stauber WT. Eccentric action of muscles: physiology, injury, and adaptation. Exerc Sport Sci Rev. 1989;17:157–85.
6. Benedict FG, Parmenter HS. The energy metabolism of women while ascending or descending stairs. Am J Physiol. 1928;84:675–98.
7. Okamoto T, Masuhara M, Ikuta K. Cardiovascular responses induced during high-intensity eccentric and concentric isokinetic muscle contraction in healthy young adults. Clin Physiol Funct Imaging. 2006;26:39–44.
8. Vallejo AF, Schroeder ET, Zheng L, Jensky NE, Sattler FR. Cardiopulmonary responses to eccentric and concentric resistance exercise in older adults. Age Ageing. 2006;35:291–7.
9. Perrey S, Betik A, Candau R, Rouillon, Hughson RL. Comparison of oxygen uptake kinetics during concentric and eccentric cycle exercise. J Appl Physiol. 2001;91:2135–42.
10. Overend TJ, Versteegh TH, Thompson E, Birmingham TB, Vandervoort AA. Cardiovascular stress associated with concentric and eccentric isokinetic exercise in young and older adults. J Gerontol A Biol Sci Med Sci. 2000;55:B177–82.
11. Knuttgen, HG, Petersen FB, Klausen K. Oxygen uptake and heart rate responses to exercise performed with concentric and eccentric muscle contractions. Med Sci Sport Exerc. 1971;3:1–5.
12. Chung F, Dean E, Ross J. Cardiopulmonary responses of middle-aged men without cardiopulmonary disease to steady-rate positive and negative work performed on a cycle ergometer. Phys Ther. 1999;79:476–87.
13. Horstmann T, Mayer F, Maschmann J, Niess A, Roecker K, Dickhuth HH. Metabolic reaction after concentric and eccentric endurance-exercise of the knee and ankle. Med Sci Sport Exerc. 2001;33:791–5.
14. Lindstedt SL, LaStayo PC, Reich TE. When active muscles lengthen: properties and consequences of eccentric contractions. News Physiol Sci. 2001;16:256–61.
15. Lindstedt SL, Reich TE, Keim P, LaStayo PC. Do muscles function as adaptable locomotor springs? J Exp Biol. 2002;205:2211–6.
16. Reich TE, Lindstedt SL, LaStayo PC, Pierotti DJ. Is the spring quality of muscle plastic? Am J Physiol Regul Integr Comp Physiol. 2000;278:1661–6.
17. Taylor C. Force development during sustained locomotion: a determinant of gait, speed and metabolic power. J Exp Biol. 1985;115:253–62.
18. Tesch PA, Dudley GA, Duvoisin MR, Hather BM, Harris RT. Force and EMG signal patterns during repeated bouts of concentric or eccentric muscle actions. Acta Physiol Scand. 1990;138:263–71.
19. Goldberg AL, Etlinger JD, Goldspink DF, Jablecki C. Mechanism of work-induced hypertrophy of skeletal muscle. Med Sci Sport Exerc. 1975;7:185–98.
20. Johnson BL, Adamczyk JW, Tennoe KO, Stromme SB. A comparison of concentric and eccentric muscle training. Med Sci Sport Exerc. 1976;8:35–8.
21. Higbie EJ, Cureton KJ, Warren GL, Prior BM. Effects of concentric and eccentric training on muscle strength, cross-sectional area, and neural activation. J Appl Physiol. 1996;81:2173–81.
22. Duncan PW, Chandler JM, Cavanaugh DK, Johnson KR, Buehler AG. Mode and speed specificity of eccentric and concentric exercise training. J Orthop Sports Phys Ther. 1989;11:70–5.
23. Dudley GA, Tesch PA, Millar BJ, Buchanan P. Importance of eccentric actions in performance adaptations to resistance training. Aviat Space Environ Med. 1991;62:543–50.

24. Hilliard-Robertson PC, Schneider SM, Bishop SL, Guilliams ME. Strength gains following different combined concentric and eccentric exercise regimens. Aviat Space Environ Med. 2003;74:342–7.
25. Walker PM, Brunotte F, Rouhier-Marcer I, Cottin Y, Casillas JM, Gras P, et al. Nuclear magnetic resonance evidence of different muscular adaptations after resistance training. Arch Phys Med Rehabil. 1998;79:1391–8.
26. Seger JY, Arvidsson B, Thorstensson A. Specific effects of eccentric and concentric training on muscle strength and morphology in humans. Eur J Appl Physiol. 1998;79:49–57.
27. Hortobágyi T, Barrier J, Beard D, Braspennincx J, Koens P, Devita P, et al. Greater initial adaptations to submaximal muscle lengthening than maximal shortening. J Appl Physiol. 1996;81:1677–82.
28. Hortobágyi T, Hill JP, Houmard JA, Fraser NJ, Lambert NJ, Israel RG. Adaptive responses to muscle lengthening and shortening in humans. J Appl Physiol. 1996;80:765–72.
29. LaStayo PC, Pierotti DD, Pifer J, Hoppeler H, Lindstedt SL. Eccentric ergometry: increases in locomotor muscle size and strength at low training intensities. Am J Physiol Regul Integr Comp Physiol. 2000;278:R1282–8.
30. Hortobágyi T, Devita P. Favorable neuromuscular and cardiovascular responses to 7 days of exercise with an eccentric overload in elderly women. J Gerontol A Biol Sci Med Sci. 2000;55A:B401–10.
31. Hortobágyi T, Zheng D, Weidner M, Lambert NJ, Westbrook S, Houmard JA. The influence of aging on muscle strength and muscle fiber characteristics with special reference to eccentric strength. J Gerontol A Biol Sci Med Sci. 1995;50A:B399–406.
32. Krishnathasan D, Vandervoort AA. Eccentric strength training prescription for older adults. Top Geriatr Rehabil. 2000;15:29–40.
33. LaStayo PC, Ewy GA, Pierotti DD, Johns RK, Lindstedt S. The positive effects of negative work: increased muscle strength and decreased fall risk in a frail elderly population. J Gerontol A Biol Sci Med Sci. 2003;58:M419–24.
34. Dibble LE, Hale T, Marcus RL, Gerber JP, LaStayo PC. The safety and feasibility of high-force eccentric resistance exercise in persons with Parkinson's disease. Arch Phys Med Rehabil. 2006;87:1280–2.
35. Gür H, Cakun N, Akova B, Okay E, Küçukoglu S. Concentric versus combined concentric-eccentric isokinetic training: effects on functional capacity and symptoms in patients with osteoarthrosis of the knee. Arch Phys Med Rehabil. 2002;83:308–16.
36. Steiner R, Meyer K, Lippuner K, Schmid JP, Saner H, Hoppeler H. Eccentric endurance training in subjects with coronary artery disease: a novel exercise paradigm in cardiac rehabilitation? Eur J Appl Physiol. 2004;91:572–8.
37. Debigaré R, Coté CH, Maltais F. Peripheral muscle wasting in chronic obstructive pulmonary disease: clinical relevance and mechanisms. Am J Respir Crit Care Med. 2001;164:1712–7.
38. MacIntyre RN. Muscle dysfunction associated with chronic obstructive pulmonary disease. Respir Care. 2006;51:840–52.
39. Harrington D, Anker SD, Chua TP. Skeletal muscle function and its relation to exercise tolerance in chronic heart failure. J Am Coll Cardiol. 1997;30:1758–64.
40. Piepoli MF, Scott AC, Capucci A, Coats AJS. Skeletal muscle training in chronic heart failure. Acta Physiol Scand. 2001;171:295–303.
41. Metoki N, Yoshihiro S, Kei S, Okumura K, Iwamoto J. Muscular atrophy in the hemiplegic thigh in patients after stroke. Am J Phy Med Rehabil. 2003;82:862–5.
42. Ryan AS, Dobrovolny CL, Smith GV, Silver KH, Macko RF. Hemiparetic muscle atrophy and increased intramuscular fat in stroke patients. Arch Phys Med Rehabil. 2002;83:1703–7.
43. Serres I, Hayot M, Préfaut C, Mercier J. Skeletal muscle abnormalities in patients with COPD: contribution to exercise intolerance. Med Sci Sport Exerc. 1998;30:1019–27.
44. Polkey, MI. Muscle metabolism and exercise tolerance in COPD. Chest. 2002;121:131s–5s.
45. Mancini D, Walter G, Reichek N, Lenkinski R, McCully KK, Mullen JL. Contribution of skeletal muscle atrophy to exercise intolerance and altered muscle metabolism in heart failure. Circulation. 1992;85:1364–73.
46. LeBrasseur NK, Sayers SP, Ouellette MM, Fielding RA. Muscle impairments and behavioural factors mediate functional limitations and disability following stroke. Phys Ther. 2006;86:1342–50.
47. Hunter GR, McCarthy JP, Bamman M. Effects of resistance training on older adults. Sports Med. 2004;34:329–48.
48. Trappe S, Williamson D, Godard M, Porter D, Rowden G, Costill D. Effect of resistance training on single muscle fiber contractile function in older men. J Appl Physiol. 2000;89:143–52.
49. Klitgaard H, Mantoni M, Schiaffino S, Ausoni S, Gorza L, Laurent-Winter C, et al. Function, morphology and protein expression of ageing skeletal muscle: a cross-sectional study of elderly men with different training backgrounds. Acta Physiol Scand. 1990;140:41–54.
50. Lemura LM, von Duvillard SP. Clinical exercise physiology. Philadelphia: Lippincott Williams & Wilkins; 2004.
51. Durstine JL, Moore GE. ACSM's exercise management for persons with chronic diseases and disabilities. Champaign, IL: Human Kinetics; 2003.
52. Timmreck TC. Dictionary of health services management. 2nd ed. Boston: National Health Publications; 1986.
53. Sackett DL. Rules of evidence and clinical recommendations for the use of antithrombotic agents. Chest. 1986;89:2s–3s.
54. Barry MJ. Evidence-based practice in pediatric physical therapy. PT Magazine. 2001;9:175–81.
55. Centre for Evidence-Based Medicine [homepage on the Internet]. Oxford: The Centre; n.d. [cited 2007 May 11]. Levels of evidence [1 screen]. Available from: http://www.cebm.net/levels_of_evidence.asp.
56. Medlicott MS, Harris SR. A systematic review of the effectiveness of exercise, manual therapy, electrotherapy, relaxation training, and biofeedback in the management of temporomandibular disorder. Phys Ther. 2006;86:955–73.
57. Portney LG, Watkins MP. Foundations of clinical research: applications to practice. 2nd ed. Upper Saddle River, NJ: Prentice Hall; 2000.
58. Physiotherapy Evidence Database (PEDro) [homepage on the Internet]. Sydney: PEDro; 1999 [updated 1999 Mar; cited 2007 May 11]. PEDro scale [about 4 screens]. Available from: http://www.pedro.fhs.usyd.edu.au/scale_item.html.

59. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys Ther. 2003;83:713–21.
60. Tooth L, Bennett S, McCluskey A, Hoffmann T, McKenna K, Lovarini M. Appraising the quality of randomized controlled trials: inter-rater reliability for the OTseeker evidence database. J Eval Clin Pract. 2005;11:547–55.
61. Verhagen AP, de Vet HCW, de Bie RA, Kessels AG, Borres M, Bouter LM, et al. The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. J Clin Epidemiol. 1998;51:1235–41.
62. Cohen J. Statistical power analysis for the behavioural sciences. 2nd ed. Hillsdale, NJ: Lawrence Erlbaum; 1998.
63. Rooyackers JM, Berkeljon DA, Folgering HTM. Eccentric exercise training in patients with chronic obstructive pulmonary disease. Int J Rehabil Res. 2003;26:47–9.
64. Meyer K, Steiner R, Lastayo P, Lippuner K, Allemann Y, Eberli F, et al. Eccentric exercise in coronary patients: central hemodynamic and metabolic responses. Med Sci Sport Exerc. 2003;35:1076–82.
65. Dibble L, Hale TF, Marcus RL, Droge J, Gerber JP, LaStayo PC. High-intensity resistance training amplifies muscle hypertrophy and functional gains in persons with Parkinson's disease. Mov Disord. 2006;21:1444–52.
66. Harris-Love MO. Safety and efficacy of submaximal eccentric strength training for a subject with polymyositis. Arthritis Rheum. 2005;53:471–4.
67. Zoll J, Steiner R, Meyer K, Vogt M, Hoppeler H, Flück M. Gene expression in skeletal muscle of coronary artery disease patients after concentric and eccentric endurance training. Eur J Appl Physiol. 2006;96:413–22.
68. Engardt M, Knutsson E, Jonsson M, Sternhag M. Dynamic muscle strength training in stroke patients: effects on knee extension torque, electromyographyc activity and motor function. Arch Phys Med Rehabil. 1995;76:419–25.
69. Connelly DM, Vandervoort AA. Effects of isokinetic strength training on concentric and eccentric torque development in the ankle dorsiflexors of older adults. J Gerontol A Biol Sci Med Sci. 2000;55:B465–72.
70. Lastayo PC, Jons R, McDonagh P, Lindstedt SL. High force eccentric exercise for sarcopenia. Sixth IOC World Congress on Sport Sciences, St Louis, Missouri, USA; 2002 Jun 1. N.p.: International Olympic Committee; 2002. p. 96.
71. Bertovic DA, Waddell TK, Gatzka CD, Cameron JD, Dart AM, Kingwell BA. Muscular strength training is associated with low arterial compliance and high pulse pressure. Hypertension. 1999;33:1385–91.
72. Okamoto T, Masuhara M, Ikuta K. Effects of eccentric and concentric resistance training on arterial stiffness. J Hum Hypertens. 2006;20:348–54.
73. Carrasco DI, Delp MD, Ray CA. Effect of concentric and eccentric muscle actions on muscle sympathetic nerve activity. J Appl Physiol. 1999;86:558–63.
74. Tesch PA, Thorsson A, Colliander EB. Effects of eccentric and concentric resistance training on skeletal muscle substrates, enzyme activities and capillary supply. Acta Physiol Scand. 1990;140:575–80.
75. Chen Y, Hubal MJ, Hoffman EP, Thompson PD, Clarkson PM. Molecular responses of human muscle to eccentric exercise. J Appl Physiol. 2003;95:2485–94.
76. Nielsen B, Nielsen SL, Bonde-Petersen F. Thermoregulation during positive and negative work at different environmental temperatures. Acta Physiol Scand. 1972:85:249–57.
77. Knuttgen HG, Nadel ER, Pandolf KB, Patton JF. Effects of training with eccentric muscle contractions on exercise performance, energy expenditure, and body temperature. Int J Sports Med. 1982;3:3–7.
78. Dean E. Physiology and therapeutic implications of negative work: a review. Phys Ther. 1988:68:233–8.
79. Ouellette MM, LeBrasseur NK, Bean JF. High-intensity resistance training improves muscle strength, self-reported function, and disability in long-term stroke survivors. Stroke. 2004;35:1404–9.
80. Teixeira-Salmela LF, Olney SJ, Nadeau S, Brouwer B. Muscle strengthening and physical conditioning to reduce impairment and disability in chronic stroke survivors. Arch Phys Med Rehabil. 1999;80:1211–8.
81. Patten C, Lexell J, Brown HE. Weakness and strength training in persons with post-stroke hemiplegia: rationale, method and efficacy. J Rehabil Res Dev. 2004;41: 293–312.
82. Knutsson E. Concentric and eccentric muscle work in spastic paresis. Scand J Rehab Med. 1992;24(Suppl):16–7.
83. Fridén J. Changes in human skeletal muscle induced by long-term eccentric exercise. Cell Tissue Res. 1984;236: 365–72.
84. Barry B, Carson RG. The consequences of resistance training for movement control in older adults. J Gerontol A Biol Sci Med Sci. 2004;59A:730–54.
85. Rhodes E, Martin AD, Taunton JE, Donnelly M, Warren J, Elliot J. Effects of one year of resistance training on the relation between muscular strength and bone density in elderly women. Brit J Sport Med. 2000;34:18–22.
86. Hawkins SA, Schroeder ET, Wiswell RA, Jaque SV, Marcell TJ, Costa K. Eccentric muscle action increases site-specific osteogenic response. Med Sci Sport Exerc. 1999;31:1287–92.
87. Hubal MJ, Ingalls CP, Allen MR, Wenke JC, Hogan HA, Bloomfield SA. Effects of eccentric exercise training on cortical bone and muscle strength in the estrogen-deficient mouse. J Appl Physiol. 2005;98:1674–81.
88. Schroeder ET, Hawkins SA, Jaque SV. Musculoskeletal adaptations to 16 weeks of eccentric progressive resistance training in young women. J Strength Cond Res. 2004;18: 227–35.
89. Kilmer D, Aitkens SG, Wright NC, McCrory MA. Response to high-intensity eccentric muscle contractions in persons with myopathic disease. Muscle Nerve 2001;24:1181–7.
90. Ansved T. Muscle training in muscular dystrophies. Acta Physiol Scand. 2001;171:359–66.
91. Lieber RL. Skeletal muscle structure, function and plasticity. 2nd ed. Baltimore, MD: Lippincott, Williams & Wilkins; 2002.
92. Carter GT, Abresch RT, Fowler WM Jr. Adaptations to exercise training and contraction-induced muscle injury in animal models of muscular dystrophy. Am J Phys Med Rehabil. 2002;81(Suppl):S151–61.
93. Drexel H, Loruenser G, Langer P. Effect of concentric and eccentric muscle training on glucose tolerance in healthy sedentary individuals. Z Kardio. 2004;11:277.
94. Bigland-Ritchie B, Graichen H, Woods JJ. A variable-speed motorized bicycle ergometer for positive and negative work exercise. J Appl Physiol. 1973;35:739–40.

95. Toigo M, Boutellier U. New fundamental resistance exercise determinants of molecular and cellular adaptations. Eur J Appl Physiol. 2006;97:643–63.
96. Mathur S, MacIntyre DL, Foster BB, Road JD, Levy RD, Reid WD. Preservation of eccentric torque of the knee extensors and flexors in patients with COPD. J Cardiopulm Rehabil Prev. 2007;27:411–6.
97. Lomaglio M, Eng J, MacIntyre DL. Relative preservation of eccentric strength in the paretic and non paretic leg muscles of individuals with chronic stroke. (Unpublished data).
98. Hortobágyi T. The positives of negatives: clinical implications of eccentric resistance exercise in old adults. J Gerontol A Biol Sci Med Sci. 2003;58A:417–8.
99. Sayers SP, Clarkson PM, Rouzier PA, Kamen, G. Adverse events associated with eccentric exercise protocols: six case studies. Med Sci Sport Exerc. 1999;31: 1697–702.
100. Rader EP, Faulkner JA. Effect of aging on the recovery following contraction-induced injury in muscles of female mice. J Appl Physiol. 2006;101:887–92.